

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

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Applicant's or agent's file reference PCT 21069	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US03/09274	International filing date (<i>day/month/year</i>) 27 March 2003 (27.03.2003)	Priority date (<i>day/month/year</i>) 29 March 2002 (29.03.2002)
International Patent Classification (IPC) or national classification and IPC IPC(7): C12Q 1/70; C12N 7/00; A61K 31/395 and US Cl.: 435/5, 235.1; 424/233.1		
Applicant MERCK & CO., INC.		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>4</u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u> </u> sheets.</p> <p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input type="checkbox"/> Non-establishment of report with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input checked="" type="checkbox"/> Certain observations on the international application 		
Date of submission of the demand 20 October 2003 (20.10.2003)	Date of completion of this report 19 July 2004 (19.07.2004)	
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 872-9306	Authorized officer <i>Cherise Bell-Harris</i> Stacy B. Chen Telephone No. (571) 272-1600	

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US03/09274

I. Basis of the report

1. With regard to the elements of the international application:*

☒ the international application as originally filed.☒ the description:

pages 1-32 as originally filed

pages NONE, filed with the demand

pages NONE, filed with the letter of _____

☒ the claims:

pages 33-38 as originally filed

pages NONE, as amended (together with any statement) under Article 19

pages NONE, filed with the demand

pages NONE, filed with the letter of _____

☒ the drawings:

pages 1-9 as originally filed

pages NONE, filed with the demand

pages NONE, filed with the letter of _____

☐ the sequence listing part of the description:

pages NONE as originally filed

pages NONE, filed with the demand

pages NONE, filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).☐ the language of publication of the international application (under Rule 48.3(b)).☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in printed form.☐ filed together with the international application in computer readable form.☐ furnished subsequently to this Authority in written form.☐ furnished subsequently to this Authority in computer readable form.☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.4. ☐ The amendments have resulted in the cancellation of:☐ the description, pages NONE☐ the claims, Nos. NONE☐ the drawings, sheets/fig NONE5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US03/09274**V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. STATEMENT**

Novelty (N)	Claims <u>NONE</u>	YES
	Claims <u>1-46</u>	NO
Inventive Step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-46</u>	NO
Industrial Applicability (IA)	Claims <u>1-46</u>	YES
	Claims <u>NONE</u>	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-46 lack novelty and inventive step under PCT Article 33(2) and (3) as being anticipated by and suggested by Zhang *et al* (5,194,191 B1). The claims are drawn to a method of large scale virus production comprising inoculating a cell growth medium that contains a shear-protective compound, culturing the cells, infecting with virus seed stock, culturing viruses under gas sparging, harvesting virus and purifying virus. The shear-protective compound can be Pluronic®F-68. The virus can be adenovirus. Also claimed is a method of producing a virus seed stock, such as adenovirus, free of cell-lysis components. The mechanical shearing alternative can be hollow fiber ultrafiltration. Also claimed is a virus seed stock, such as adenovirus.

Zhang teaches a method for the production and purification of adenoviral vectors comprising growing host cells, infecting with adenovirus, harvesting and lysing using a method such as impinging jets and hollow fiber ultrafiltration (col. 2, lines 58-61 and col. 12, line 49). Gas sparging can be used in Zhang's method (col. 11, lines 1-11). Pluronic®F-68 (0.1%) can be used in the culture (col. 4, lines 25-28). Also taught are methods of purification of adenovirus from cell lysates, such as clarification, concentration and diafiltration. Therefore, the invention is anticipated by and suggested by the prior art.

Claims 1-46 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

----- NEW CITATIONS -----

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

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VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claims 2-5, 8-15, 17-20 and 25-30 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claims 2-5, 8-15, 17-20 and 25-30 are indefinite for the following reason(s): The use of the trademark Pluronic®F-68 renders the claims indefinite because the exact formula of a trademark such as Pluronic®F-68 may be altered at any time. The claims have been searched only with regard to the trademark name.